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Article

Frequency of Disease-Free and Overall Survival Outcomes in Triple-Negative Breast Cancer Patients Following Neoadjuvant Chemotherapy

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ABSTRACT

Background: Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype with limited treatment options due to the absence of hormonal receptors. While achieving a pathological complete response (pCR) after neoadjuvant chemotherapy (NACT) is associated with favorable outcomes, there remains a need to evaluate survival patterns and residual risk factors, particularly in low- and middle-income regions where data are scarce. **Objective**: This study aimed to determine the frequency of disease-free survival (DFS) and overall survival (OS) at 12 months among stage II and III TNBC patients who achieved pCR following NACT and underwent modified radical mastectomy (MRM), and to identify clinicopathological variables influencing these outcomes. **Methods**: A descriptive case series was conducted at INMOL Hospital, Lahore, involving 150 female TNBC patients aged 18–60 years who achieved pCR post-NACT and underwent MRM. Patients were selected based on defined clinical and pathological criteria. Data on demographic, treatment, and pathological parameters were collected, and DFS and OS at 12 months were recorded. Ethical approval was obtained in accordance with the Declaration of Helsinki. Statistical analysis was performed using SPSS version 27, applying descriptive statistics, chi-square tests, and logistic regression to evaluate associations. **Results**: At 12-month follow-up, DFS and OS were 88.0% and 96.0%, respectively. Surgical margin positivity was significantly associated with reduced DFS ($p = 0.001$), while lymph node involvement was linked with decreased OS ($p = 0.015$). BMI, comorbidities, and tumor size showed no significant associations with survival outcomes. **Conclusion**: TNBC patients achieving pCR after NACT demonstrate high short-term survival; however, surgical margin status and nodal burden remain critical prognostic factors. These findings highlight the need for meticulous surgical planning and tailored postoperative surveillance to optimize outcomes in high-risk TNBC subgroups.

Keywords: Triple-Negative Breast Neoplasms, Neoadjuvant Therapy, Pathologic Complete Response, Survival Rate, Mastectomy, Disease-Free Survival, Lymphatic Metastasis.

INTRODUCTION

Triple-negative breast cancer (TNBC) represents one of the most aggressive subtypes of breast malignancies, characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression. Globally, breast cancer remains the most commonly diagnosed cancer in women, with an estimated 2.3 million new cases and approximately 685,000 deaths annually (1). Among these, TNBC accounts for 12–20% and is particularly known for its high histologic grade, early recurrence patterns, and poor overall prognosis due to limited targeted treatment options (2,3). Because TNBC lacks the biological targets amenable to hormone or HER2-directed therapies, systemic chemotherapy remains the cornerstone of its treatment, especially in the early stages. In recent years, neoadjuvant chemotherapy (NACT) has emerged as a preferred approach over adjuvant chemotherapy in managing TNBC, offering benefits such as early control of micro metastatic disease, tumor downstaging, and potential eligibility for breast-conserving surgery (4,5). Achieving a pathological complete response (pCR) following NACT is particularly prognostic in TNBC, with studies demonstrating significant survival advantages in patients who attain pCR. For instance, Fisher et al.

reported a 92.3% overall survival (OS) rate in patients achieving pCR compared to those with residual disease (6). Similarly, Chen et al. found that the five-year disease-free survival (DFS) was markedly higher in patients with pCR (95.3%) versus non-pCR cases (72.7%)(7). Shao et al. and Sharma et al. also demonstrated that pCR status following NACT serves as a powerful predictor of both OS and DFS (8,9). Despite these encouraging outcomes, a subset of patients still experience recurrence or death even after achieving pCR, underscoring the heterogeneity of TNBC and the need for further investigation into survival determinants.

Although the prognostic role of pCR is well established, limited studies in the South Asian context have specifically evaluated survival outcomes following NACT among stage II and III TNBC patients who achieved pCR. Most existing literature either combines all breast cancer subtypes or does not account for the influence of local surgical and follow-up practices. Moreover, variations in lymph node involvement, tumor size, and comorbidities such as diabetes and hypertension may influence survival outcomes even among pCR achievers, warranting detailed subgroup analysis. This gap highlights the need for local data to validate international findings and to inform context-specific management strategies.

Given the aggressive nature of TNBC and the prognostic implications of pCR following NACT, this study seeks to determine the frequency of disease-free and overall survival at 12 months in patients with TNBC who achieved pCR and underwent modified radical mastectomy. By assessing real-world survival rates and their association with clinical and pathological variables, this study aims to enhance our understanding of early outcomes in this high-risk cohort. The central research question is: What is the frequency of 12-month DFS and OS in stage II and III TNBC patients with pCR following neoadjuvant chemotherapy and surgery, and which clinical factors are associated with these outcomes?

MATERIAL AND METHODS

This study was a descriptive case series conducted at the Department of Medical Oncology, INMOL Hospital, Lahore, over a duration of nine months following approval of the research protocol. Female patients aged 18 to 60 years, diagnosed with stage II or III triple-negative breast cancer (TNBC) confirmed by immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH), were included. Eligible patients had completed a full course of neoadjuvant chemotherapy (NACT) and subsequently underwent modified radical mastectomy (MRM), achieving pathological complete response (pCR) as determined by histopathological analysis.

Patients were excluded if they had received any prior systemic treatment for breast cancer aside from NACT, showed signs of disease recurrence or metastasis following NACT, or had significant comorbid conditions such as uncontrolled diabetes, cardiovascular disease, or active infection. Patients who did not complete the full NACT protocol, were lost to follow-up, or developed distant metastases during treatment were also excluded. Participant eligibility was confirmed by reviewing clinical records, pathology reports, and treatment documentation. Informed consent was obtained from all participants, and confidentiality was maintained by de-identifying patient data and securing research documents in password-protected systems.

The primary outcomes were disease-free survival (DFS) and overall survival (OS) at 12 months. DFS was defined as the duration from the initiation of NACT to the occurrence of disease recurrence or a new primary breast cancer. OS was defined as the duration from the start of NACT to death from any cause. Both outcomes were recorded at the end of the 12-month period. DFS and OS were assessed using clinical examination, medical record follow-up, and where indicated, imaging studies such as CT scans. Baseline characteristics including age, BMI, comorbid conditions (diabetes mellitus, hypertension), smoking status, tumor size, lymph node involvement, and margin status were also collected using a structured data proforma. All patients included in the final analysis had achieved pCR and completed the planned surgical and chemotherapeutic treatment protocol. Follow-up status was verified via outpatient records and telephonic interviews to document survival and recurrence outcomes.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from the institutional review board prior to study initiation. All participants provided written informed consent, and their confidentiality was preserved through coded data entries without personal identifiers. Statistical analysis was performed using IBM SPSS Statistics version 27. Categorical variables including stage of cancer, comorbidity status, margin status, and survival outcomes were reported as frequencies and percentages. Continuous variables such as age, height, and weight were summarized as mean and standard deviation. Chi-square tests were applied to evaluate associations between categorical variables and the primary outcomes (DFS and OS). Confounding variables such as age, BMI, comorbidities, and cancer stage were controlled through stratification, and p-values less than 0.05 were considered statistically significant (1).

RESULTS

A total of 150 patients diagnosed with stage II or III triple-negative breast cancer (TNBC) who achieved pathological complete response (pCR) following neoadjuvant chemotherapy (NACT) and underwent modified radical mastectomy (MRM) were included in the final analysis. The mean height of the cohort was 160.83 ± 5.85 cm, and the mean weight was 72.03 ± 8.96 kg (Table 1). In terms of body mass index (BMI) categories, the majority of patients were classified as overweight (n = 88, 58.7%) or obese (n = 35, 23.3%), with only 18% falling within the normal weight category. Current smokers constituted 23.3% of the sample, while the remaining 76.7% had never smoked.

Comorbid conditions were present in a substantial proportion of patients, with diabetes mellitus (DM) observed in 24% (n = 36) and hypertension (HTN) in 25.3% (n = 38). Stage II disease was more common (n = 86, 57.3%) compared to stage III (n = 64, 42.7%). Diagnostic confirmation of TNBC was predominantly through immunohistochemistry (IHC) (n = 111, 74%), with fewer patients diagnosed via FISH (6.7%) or both modalities (19.3%). Nearly all patients completed the prescribed NACT regimen (n = 139, 92.7%). Regarding nodal burden, 90.7% had N1 (1–3 lymph nodes)

involvement, and 9.3% were node-negative (N0). Tumor size was primarily within the T2 category (n = 135, 90%) while T1 tumors accounted for 10%. Most patients had negative surgical margins (n = 142, 94.7%). Distant metastases (M1) were present in 12.7% of cases (Table 2). At 12-month follow-up, the disease-free survival (DFS) rate was 88.0% (n = 132), while overall survival (OS) was 96.0% (n = 144). Chi-square tests were conducted to evaluate associations between clinical variables and DFS or OS outcomes.

Table 1. Descriptive Statistics for Continuous Variables (n = 150)

Variable	Mean ± SD
Height (cm)	160.83 ± 5.85
Weight (kg)	72.03 ± 8.96

Table 2. Categorical Variables with Frequencies, Percentages, and p-values for DFS12mo and OS12mo

Variable	Category	n (%)	p-value (DFS12mo)	p-value (OS12mo)
BMI Group	Normal	27 (18.0%)	0.374	0.111
	Overweight	88 (58.7%)		
	Obese	35 (23.3%)		
Smoking Status	Current Smoker	35 (23.3%)	0.191	–
	Never Smoked	115 (76.7%)		
Diabetes Mellitus	No	114 (76.0%)	0.172	0.585
	Yes	36 (24.0%)		
Hypertension	No	112 (74.7%)	0.139	0.145
	Yes	38 (25.3%)		
Cancer Stage	Stage II	86 (57.3%)	0.730	0.711
	Stage III	64 (42.7%)		
Diagnostic Method	IHC	111 (74.0%)	0.345	–
	FISH	10 (6.7%)		
	Both	29 (19.3%)		
Dose Completed	Complete	139 (92.7%)	0.512	–
	Incomplete	11 (7.3%)		
Lymph Node Score	N0	14 (9.3%)	0.782	0.039
	N1 (1–3 nodes)	136 (90.7%)		
Tumor Size	T1	15 (10.0%)	0.503	0.579
	T2	135 (90.0%)		
Node Involvement	N0	95 (63.3%)	0.061	0.015
	N1	55 (36.7%)		
Surgical Margin	Negative	142 (94.7%)	0.001	–
	Positive	8 (5.3%)		
Metastasis	M0	131 (87.3%)	–	0.764
	M1	19 (12.7%)		

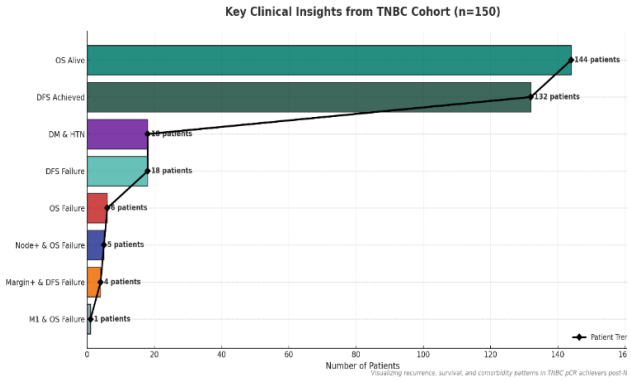

Figure 1 Key Clinical Insights from TNBC Cohort (n=150)"

In contrast, OS at 12 months demonstrated statistically significant associations with lymph node score (χ^2 = 4.25, df = 1, p = 0.039) and nodal involvement (χ^2 = 5.86, df = 1, p = 0.015), both indicating a poorer survival rate in patients with more extensive lymph node burden. No statistically significant relationships were observed between BMI category, smoking status, DM, HTN, tumor size, or cancer stage and either DFS or OS (all p > 0.05). These findings suggest that while most patients with TNBC achieving pCR experience favorable short-term survival, margin status and lymph node burden remain critical prognostic indicators

DISCUSSION

The present study evaluated disease-free and overall survival outcomes at 12 months in a cohort of patients with stage II and III triple-negative breast cancer (TNBC) who achieved pathological complete response (pCR) following neoadjuvant chemotherapy (NACT) and underwent modified radical

mastectomy (MRM). The findings demonstrated favorable short-term outcomes, with an 88% disease-free survival (DFS) and a 96% overall survival (OS) rate. These results underscore the prognostic importance of pCR in TNBC and align with earlier studies that have identified pCR as a strong surrogate marker for improved long-term survival. For instance, Fisher et al. reported a 92.3% OS in patients with TNBC achieving pCR following NACT (6), while Chen et al. found that patients with pCR had a significantly better 5-year DFS and OS compared to those with residual disease (7). Similarly, Sharma et al. noted a recurrence-free survival of 98% in TNBC patients undergoing NACT with pCR at a median follow-up of 37 months (9). The consistent trends across diverse cohorts reinforce the clinical utility of achieving pCR as a key therapeutic milestone in TNBC management.

Notably, this study contributes novel insights by examining recurrence and survival patterns exclusively in pCR-achieving patients, thus isolating prognostic variables beyond chemotherapy responsiveness. Surgical margin positivity was significantly associated with reduced DFS ($p = 0.001$), highlighting the importance of achieving ontologically clear margins even in the context of pCR. This observation supports prior evidence suggesting that residual microscopic disease at the surgical margin may predispose to local recurrence despite apparent systemic tumor clearance (10-13). Additionally, lymph node burden, reflected through both lymph node scores and nodal involvement, demonstrated a statistically significant impact on OS ($p = 0.039$ and $p = 0.015$, respectively), suggesting that nodal status retains prognostic significance even when primary tumors have fully responded to chemotherapy. This may be explained by the presence of undetected micro metastases or the immunologic and molecular complexity of nodal disease in TNBC (4, 14).

Interestingly, no statistically significant associations were found between DFS or OS and variables such as body mass index (BMI), diabetes mellitus, hypertension, smoking status, or tumor size. These findings, while partially consistent with previous reports, also suggest that traditional prognostic indicators may have limited predictive power in the specific subgroup of pCR-achieving TNBC patients. For example, while obesity has been reported to correlate with poorer breast cancer outcomes, its effect may be mitigated in patients with high chemotherapy sensitivity and complete pathological response (8). The absence of significant associations with comorbidities could also reflect stringent selection criteria or the relatively short follow-up period in this cohort (15).

From a mechanistic standpoint, the association of positive surgical margins and nodal disease with adverse outcomes, even in pCR achievers, raises questions about the biological heterogeneity within TNBC subtypes. It is plausible that certain tumors achieve pCR in the breast yet harbor resistant clones in nodal or microscopic systemic reservoirs. This underscores the potential need for molecular stratification of TNBC beyond receptor status alone, perhaps integrating genomic profiling, immune infiltration patterns, or residual cancer burden indices to refine risk prediction (13).

Clinically, the study reinforces the critical role of achieving and verifying surgical completeness and assessing nodal status as part of postoperative decision-making, even in patients with radiologic or pathological evidence of robust response. These findings advocate for meticulous surgical technique, comprehensive nodal assessment, and perhaps the consideration of adjuvant treatment in select pCR patients with high-risk features (16).

Among the strengths of this study are its focused design on a well-defined TNBC population with confirmed pCR and the inclusion of real-world data from a tertiary care oncology center, contributing valuable regional evidence. However, limitations must be acknowledged. The sample size, although adequate for descriptive and bivariate analysis, may limit the power to detect small effect sizes in multivariate models. The study's observational design precludes causal inference, and the 12-month follow-up duration restricts conclusions regarding long-term survival and late recurrences. Furthermore, the findings may not be generalizable to non-pCR TNBC populations or settings with differing surgical and chemotherapeutic protocols. Future research should aim to validate these findings in larger, multicentric cohorts with extended follow-up periods and incorporate molecular biomarkers to elucidate the biological underpinnings of residual risk in pCR-achieving TNBC patients. Additionally, prospective studies evaluating the benefit of tailored adjuvant therapies in high-risk pCR subsets may further refine personalized treatment approaches in this challenging cancer subtype (12, 16).

CONCLUSION

This study demonstrated that among patients with stage II and III triple-negative breast cancer who achieved pathological complete response following neoadjuvant chemotherapy and underwent modified radical mastectomy, the 12-month disease-free and overall survival outcomes were notably high, at 88% and 96%, respectively. However, the presence of positive surgical margins and lymph node involvement remained significantly associated with reduced survival, underscoring the continued relevance of these pathological factors even in pCR-achieving patients. These findings highlight the importance of comprehensive surgical clearance and nodal assessment in optimizing early survival outcomes and support the integration of postoperative risk stratification in clinical decision-making. Clinically, the results emphasize that pCR alone may not fully predict prognosis in TNBC, while from a research perspective, they warrant further investigation into the molecular and immune profiles of residual risk in this high-risk subgroup to guide precision oncology strategies.

REFERENCES

1. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and Future Burden of Breast Cancer: Global Statistics for 2020 and 2040. Breast. 2022;66:15–23.

2. Anders CK, Carey LA. Biology, Metastatic Patterns, and Treatment of Patients With Triple-Negative Breast Cancer. Clin Breast Cancer. 2009;9(Suppl 2):S73–81.

3. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive Analysis of Estrogen Receptor (ER)-Negative, Progesterone Receptor (PR)-Negative, and HER2-Negative

Invasive Breast Cancer: A Population-Based Study From the California Cancer Registry. Cancer. 2007;109(9):1721–8.

4. Xia LY, Hu QL, Zhang J, Xu WY, Li XS. Survival Outcomes of Neoadjuvant Versus Adjuvant Chemotherapy in Triple-Negative Breast Cancer: A Meta-Analysis of 36,480 Cases. World J Surg Oncol. 2020;18(1):1–8.

5. Almansour NM. Triple-Negative Breast Cancer: A Brief Review About Epidemiology, Risk Factors, Signaling Pathways, Treatment and Role of Artificial Intelligence. Front Mol Biosci. 2022;9:836417.

6. Fisher CS, Ma CX, Gillanders WE, Aft RL, Eberlein TJ, Gao F, et al. Neoadjuvant Chemotherapy Is Associated With Improved Survival Compared With Adjuvant Chemotherapy in Patients With Triple-Negative Breast Cancer Only After Complete Pathologic Response. Ann Surg Oncol. 2012;19(1):253–8.

7. Li M, Zhou S, Lv H, Cai M, Shui R, Yang W. Neoadjuvant chemotherapy response in androgen receptor-positive triple-negative breast cancer: potential predictive biomarkers and genetic alterations. Breast Cancer Research. 2025 Dec;27(1):1-4.

8. Chen D, Wang Q, Dong M, Chen F, Huang A, Chen C, et al. Analysis of Neoadjuvant Chemotherapy for Breast Cancer: A 20-Year Retrospective Analysis of Patients of a Single Institution. BMC Cancer. 2023;23(1):1–9.

9. Shao Z, Chaudhri S, Guo M, Zhang L, Rea D. Neoadjuvant Chemotherapy in Triple Negative Breast Cancer: An Observational Study. Oncol Res. 2016;23(6):291–302.

10. Antonini M, Mattar A, Pereira TM, Oliveira LL, Teixeira MD, Amorim AG, Ferraro O, de Oliveira LC, Ramos MD, Cavalcante FP, Zerwes F. Pathologic complete response and breast cancer survival post-neoadjuvant chemotherapy: A systematic review and meta-analysis of real-world data. Heliyon. 2025 May 1;11(10).

11. Jackson I, Lei X, Malinowski C, Giordano SH, Chavez-MacGregor M. Treatment Patterns, Trends, and Outcomes of Neoadjuvant Chemotherapy Use Among Patients With Early-Stage Invasive Triple-Negative Breast Cancer. JCO Oncology Practice. 2025 Mar:OP-24.

12. Sharma P, Kimler BF, Klemp JR, Ward C, Connor CS, McGinness M, et al. Outcomes With Neoadjuvant Versus Adjuvant Chemotherapy for T1–2 Node Negative Triple Negative Breast Cancer. J Clin Oncol. 2015;33(15 Suppl):1092.

13. Liao XW, Gao JB, Sun H, Chen HD, Zheng MH, Han L, Chen XG, Su YN, Pan DL, Wu M, Cai SL. Prediction of neoadjuvant chemotherapy efficacy and prognostic biomarker analysis in patients with triple-negative breast cancer. Frontiers in Pharmacology. 2025 Mar 12;16:1553831.

14. Shigematsu H, Takaya M, Suzuki K, Fujimoto M, Ikejiri H, Amioka A, Hiraoka E, Sasada S, Arihiro K, Okada M. Exploring the possibility of omitting axillary surgery in patients with clinical node-positive breast cancer achieving ypT0 after neoadjuvant chemotherapy. Breast Cancer Research and Treatment. 2025 Apr 12:1-0.

15. Yoshino T, Zhang Z, Sato R, Lipkowitz S, Fujii T. Revisiting surrogacy of pathological complete response for long-term survival in triple-negative breast cancer. JNCI Cancer Spectrum. 2025 Apr;9(2):pkaf022.

16. Huang K, Jakub J, Gabriel E, Moreno-Aspitia A, McLaughlin S. Overall Survival Following Neoadjuvant Chemotherapy Versus Adjuvant Chemotherapy in Clinically Node Negative T1 Triple Negative Breast Cancer. Ann Surg Oncol. 2023;30(12):7026–35.